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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/603,818	06/26/2003	Thomas Nilsson	239637US0	2767

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EXAMINER	
HAGHIGHATIAN, MINA	
ART UNIT	**PAPER NUMBER**
1616	

DATE MAILED: 08/08/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/603,818	NILSSON ET AL.	
	Examiner	Art Unit	
	Mina Haghighatian	1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 June 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *18-38* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *18-38* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 06/06/06 has been entered.

Receipt is acknowledged of the Amendments, Remarks and Terminal Disclaimer filed on 06/06/06. Claims 1-17 are cancelled and new claims 18-38 are added. Accordingly claims 18-38 are pending.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 18-38 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treatment of a respiratory disorder, does not reasonably provide enablement for prophylaxis of the a respiratory disorder. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. The specification does not provide any disclosure to support a method of

preventing a respiratory disorder. This is also not known in the art. Respiratory disorders are not known to be preventable by administration of active agents such as a bronchodilator, an anti-inflammatory or combination thereof. (NOTE: Prophylaxis is defined as prevention or inhibition by Webster's dictionary and the PTO).

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 18-38 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 18 and 27 are indefinite for reciting the term "a second group of anti-inflammatory medicaments". Here, "A second... anti-inflammatory" is indefinite because there is not a first anti-inflammatory agent. Remaining claims are rejected for depending on a rejected base claim.

Claim 18 is vague and indefinite for including the term "metered pre-metered". It is not clear what the Applicant intended to claim here. Applicant is required to correct or explain on the record what is meant by the said term. Remaining claims are rejected for depending on a rejected base claim.

Claims 25 and 34 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential elements, such omission amounting to a gap between the elements. See MPEP § 2172.01. The omitted elements are: depositing a biologically acceptable, inert substance between the deposits of the medicaments.

Without the said element in claims 25 and 34 there is no substantial element to examine.

Claim Rejections - 35 USC § 103

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 18-21, 23-30 and 32-38 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gavin (WO 0178737) in view of Haikarainen et al (WO 0064519).

Gavin teaches medical combinations comprising **formoterol and budesonide**. The combinations are used for prophylaxis and treatment of respiratory diseases (see abstract). The active agents may be a racemate, solvate, hydrate or functional derivative thereof. The formulations may comprise other active agents such as **fluticasone propionate**, beclomethasone dipropionate, **mometasone furoate** or triamcinolone acetonide, sodium cromoglycate, nedocromil sodium, leukotriene antagonists, salbutamol, salmeterol, tiotropium, etc (see pages 5-6). The formulations may be in a form for inhalation such as **fine particle** dust administered via **metered dose aerosols**. Formulations for inhalation include **powder** compositions which will preferably contain lactose. The active ingredients will have a particle size of less than 100 microns, and preferably from 1 to 5 microns (see page 6).

The amounts of each active agent is disclosed in various examples, such as example 3, where **a** dry powder formulation comprises 24 microgram of (R,R)-

formoterol fumarate and 200 microgram of budesonide, thus meeting the concentration limitation of claims such as claim 7. The process of making the said formulations are disclosed in page 9 which reads "the active ingredients are micronised and bulk blended with lactose and filled into hard gelatin capsules or cartridges or in specifically constructed **double foil blister packs** to be administered by an inhaler such as a Rotahaler®, Disckhaler® or Disckus® inhaler".

Gavin, discussed above, lacks specific disclosure on the separation of the powdered active ingredients on a common dose bed.

Haikarainen teaches powder inhaler for combined medicament. The device comprises **two or more medicament containers** for different **drug powders** which are inhaled as a combined medication, and separate aerosolization channels for **each drug** powder (see abstract and page 3). The inhaler of the present invention is able to deliver and **deaggregate** medicament powder from two or more dosing recesses simultaneously without the use of pressurized air (see page 2, lines 36-38). Haikarainen also states that the first and second medicaments recess for receiving in **one position** a metered dose of the powdered medicament from the first and second medicament container (page 3, lines 24-26). The first and the second medicament containers are **separated** so that the active ingredients **can not be mixed** during storage. The suitable combinations of active agents include **formoterol and budesonide**; salmeterol and beclomethasone dipropionate; salmeterol and fluticasone, etc (see page 4).

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to have employed the method and device of Haikarainen et al to make and deliver particle formulations of two or more active agents as taught by Gavin because the method and device of Haikarainen is disclosed to be advantageous for delivering powdered combination medicaments where by storing the active agents separately, the problems of aggregation and degradation is resolved.

Claims 22 and 31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gavin (WO 0178737) in view of Haikarainen et al (WO 0064519) as applied to claims 18-21, 23-30 and 32-38 above, and further in view of Trofast (6,030,604).

The combined references discussed above, while teaching a wide variety of bronchodilators and anti-inflammatory agents, lack specific disclosure on ciclesonide.

Trofast teaches a dry powder composition comprising one or more potent pharmaceutically active substances and a carrier substance, all of which are in finely divided form. The active substance suitable for use in the invention include **ciclesonide,** formoterol, budesonide, mometasone, fluticasone, salmeterol, etc (see col. 1, lines 26-62). The particle size of the active ingredients is said to be less than 10 microns and preferably between 1 and 7 microns. The formulations comprises about 6 microgram of formoterol and 100 microgram of budesonide per unit dose (see col. 2, lines 3-10 and 15-49). The said formulations can be administered via dry powder

metered dose inhalers, to patients suffering form disorders such as respiratory disorders (col. 3, lines 20-31).

It would have been obvious to a person of ordinary skill in the art at the time the invention was made given the general teachings of the combined references, to have looked in the art for other and specific agents suitable for combination therapy such as ciclesonide, as taught by Trofast.

Double Patenting

The rejections of claims under nonstatutory double patenting based on a judicially created doctrine of obviousness over the three copending Applications are **withdrawn**. The submitted Terminal Disclaimers are entered and thus the rejections are obviated.

Response to Arguments

Applicant's arguments filed 06/06/06 have been fully considered but they are not persuasive.

Applicant argues that "Gavin describes the pharmaceutical formulation as a bulk supply, i.e. a large batch of the two medicaments mixed together, from which a pharmacist takes a patient's supply and provides as patient package". While this is a correct statement, Applicant has chosen **one** embodiment of Gavin to argue against. Gavin's reference is clearly teaching the combination of agents for aerosol delivery and

is teaching a few different ways of achieving this objection. One of these is preparing blister packages of different medicaments and administering them together or separately (see page 2, lines 1-5, page 5, lines 13-15 and page 9). Gavin's examples teaches formulations prepared in a cartridge or blister. Thus this is clearly not done by the pharmacist. Gavin also teaches using the said formulations with known commercial devices such as Rotahaler® and Disckhaler®. Thus showing that both multi- dose compartments and single blisters are known and in use.

Applicant argues that Gavin, in example 3, teaches a powder formulation where the two agents are micronized and bulk blended with lactose. This is correct, however Gavin is also teaching that compounds of the combination may be administered simultaneously, either in the **same or different** pharmaceutical **formulations** or sequentially. Specific embodiments do not negate a broader disclosure.

Applicant argues that Haikarainen teaches a multi-dose dry powder inhaler, wherein the inhaler comprises two medicament containers, each containing a supply of dry medicament powder corresponding to a multitude of metered doses. Applicant is stating that Haikarainen does not teach the common dose bed and also since the active agents are in a relatively large multi-dose containers it is difficult to keep a low moisture level in. This is not found persuasive. Haikarainen teaches a device for delivering two different powder medicaments that are stored separately, are metered into necessary doses, each dosing recess is then delivered to ONE POSITION (equivalent to a common dosing bed) and then inhaled as a combined dose. Haikarainen specifically discloses that the powders are delivered de-aggregated and are stored separately to

prevent degradation. Furthermore, the device has a lid closing the upper edge of the medicament containers and a cover together with a flap adapted to cover the medicament containers and the lid (see page 5, lines 37-39). It is then concluded that Haikarainen's device is very similar to the device claimed and that the two methods result in the same delivery of the same medicaments.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mina Haghighatian whose telephone number is 571-272-0615. The examiner can normally be reached on core office hours.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Johann Richter can be reached on 571-272-0646. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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August 03, 2006

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